

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY  
(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference HeL/AO 49909	<b>FOR FURTHER ACTION</b> See Form PCT/IPEA/416	
International application No. PCT/SE 2003/000093	International filing date (day/month/year) 21.01.2003	Priority date (day/month/year) 21.01.2002
International Patent Classification (IPC) or national classification and IPC A61K 9/20		
Applicant Galenica AB Medeon et al		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 7 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
  - a. ☐ (sent to the applicant and to the International Bureau) a total of \_\_\_\_\_ sheets, as follows:
    - ☐ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
    - ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
  - b. ☐ (sent to the International Bureau only) a total of (indicate type and number of electronic carrier(s)) \_\_\_\_\_, containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:
- |                                     |              |   |
|-------------------------------------|--------------|---|
| <input checked="" type="checkbox"/> | Box No. I    | Basis of the report   |
| <input type="checkbox"/>            | Box No. II   | Priority  |
| <input checked="" type="checkbox"/> | Box No. III  | Non-establishment of opinion with regard to novelty, inventive step and industrial applicability  |
| <input type="checkbox"/>            | Box No. IV   | Lack of unity of invention  |
| <input checked="" type="checkbox"/> | Box No. V    | Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement |
| <input type="checkbox"/>            | Box No. VI   | Certain documents cited   |
| <input type="checkbox"/>            | Box No. VII  | Certain defects in the international application  |
| <input type="checkbox"/>            | Box No. VIII | Certain observations on the international application   |

Date of submission of the demand 20.08.2003	Date of completion of this report 27.04.2004
Name and mailing address of the IPEA/SE Patent- och registreringsverket Box 5055 S-102 42 STOCKHOLM Facsimile No. +46 8 667 72 88	Authorized officer Per Renström/ELY Telephone No. +46 8 782 25 00

## Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ This report is based on a translation from the original language into the following language \_\_\_\_\_, which is the language of a translation furnished for the purposes of:

- ☐ international search (under Rules 12.3 and 23.1(b))  
☐ publication of the international application (under Rule 12.4)  
☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the **elements** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

☒ the international application as originally filed/furnished .

☐ the description:

pages \_\_\_\_\_ as originally filed/furnished  
pages\* \_\_\_\_\_ received by this Authority on \_\_\_\_\_  
pages\* \_\_\_\_\_ received by this Authority on \_\_\_\_\_

☐ the claims:

pages \_\_\_\_\_ as originally filed/furnished  
pages\* \_\_\_\_\_ as amended (together with any statement) under Article 19  
pages\* \_\_\_\_\_ received by this Authority on \_\_\_\_\_  
pages\* \_\_\_\_\_ received by this Authority on \_\_\_\_\_

☐ the drawings:

pages \_\_\_\_\_ as originally filed/furnished  
pages\* \_\_\_\_\_ received by this Authority on \_\_\_\_\_  
pages\* \_\_\_\_\_ received by this Authority on \_\_\_\_\_

☐ a sequence listing and/or any related table(s) – see Supplemental Box Relating to Sequence Listing.

3. ☐ The amendments have resulted in the cancellation of:

- ☐ the description, pages \_\_\_\_\_  
☐ the claims, Nos. \_\_\_\_\_  
☐ the drawings, sheets/figs \_\_\_\_\_  
☐ the sequence listing (*specify*): \_\_\_\_\_  
☐ any table(s) related to the sequence listing (*specify*): \_\_\_\_\_

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

- ☐ the description, pages \_\_\_\_\_  
☐ the claims, Nos. \_\_\_\_\_  
☐ the drawings, sheets/figs \_\_\_\_\_  
☐ the sequence listing (*specify*): \_\_\_\_\_  
☐ any table(s) related to the sequence listing (*specify*): \_\_\_\_\_

\* If item 4 applies, some or all of those sheets may be marked "superseded."

**Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application

☒ claims Nos. 1-9, partly

because:

☐ the said international application, or the said claims Nos. \_\_\_\_\_  
relate to the following subject matter which does not require an international preliminary examination (*specify*):

☒ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. 1-9  
are so unclear that no meaningful opinion could be formed (*specify*):

Present claims 1-9 relate to a composition-forming process which is defined in part by the properties of the substances that are incorporated into the composition, the substances used described in general terms, as well as the properties of the composition thus produced. The expressions that describe those properties (lipophilic, surfactant, lipid, filler, semi-solid, self-emulsifying, self-dispersing) are not always  
.../...

☐ the claims, or said claims Nos. \_\_\_\_\_ are so inadequately supported  
by the description that no meaningful opinion could be formed.

☐ no international search report has been established for said claims Nos. \_\_\_\_\_

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form

☐

has not been furnished

☐

does not comply with the standard

the computer readable form

☐

has not been furnished

☐

does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in the Annex C-bis of the Administrative Instructions.

☐ See Supplemental Box for further details.

## Supplemental Box

In case the space in any of the preceding boxes is not sufficient.  
Continuation of: Box III.2

explicitly used in the literature. Furthermore, support within the meaning of Article 6 PCT is to be found for only a small proportion of the compounds that fall under the properties mentioned above. Thus, a complete search of the whole scope of the claims cannot be performed.

Therefore, the search has been focused on a process which involves those compounds that are listed in the description.

Further, the search has covered the general aspects of the invention to some extent, although it lacks the necessary precision in the definition of the subject matter. Consequently, the search for the general concept of a process for the preparation of a self-dispersing or self-emulsifying tablet will retrieve a pertinent document only if this concept is described in general terms in a reference. Specific processes or tablets previously known and falling under the general concept - but failing to mention this fact - are likely not to be revealed in such a search.

Consequently, the opinion is based on the search performed.

**Box No. V** Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

## 1. Statement

Novelty (N)	Claims	<u>1-9</u>	YES
	Claims		NO
Inventive step (IS)	Claims		YES
	Claims	<u>1-9</u>	NO
Industrial applicability (IA)	Claims	<u>1-9</u>	YES
	Claims		NO

## 2. Citations and explanations (Rule 70.7)

Documents from the documents from the search report:

- A. EP0841062 A1
- B. US4935246 A1
- C. EP0455391 A2
- D. EP0911032 A1

Document A pertains to a granular preparation comprising particles prepared by melt granulation. The process further involves mixing of the particles with a low-melting oily substance, and heating the mixed powder to make the oily substance melt and bleed on the surface of the particles. The granules in reference example 1 contain an active compound, talc, lactose, corn starch and glycerol monostearate. The particles formed are mixed with talc that adheres to the surface.

Document B shows a method of coating granules. According to example 1, granules are heated until they are softened. Then, a powder mixture is added until the tackiness of the granules ceases. Suitable wax-like coating substances include fatty acids and their derivatives as well as polyethylene glycols and their derivatives. In example 2, the melt granules are composed of an active substance, paraffin wax and polyethylene glycol 6000 and the final coating contains paraffin wax and micronized lactose.

Document C discloses granules prepared by mixing a polyglycerol fatty acid ester with a powder, and heating the mixture at a temperature close to the melting point of the fatty acid ester. The polyglycerol fatty acid ester may be

.../...

## Supplemental Box

In case the space in any of the preceding boxes is not sufficient.  
Continuation of: BOX V

used in combination with a lipid. In example 9, stearate esters are mixed with an active compound. The mixture is melted and cooled. Thereafter, the mixture and corn starch are heated until the starch particles adhere to the granules.

In document D, a mixture of active compounds and a solution or melt of a fat, oily or waxy substance, and preferably an emulsifier, is made. Before drying of the mixture, fillers may be added.

Document C is considered to represent the closest prior art.

In the present application, a process for the preparation of a self-dispersing or self-emulsifying tablet is disclosed. The process involves granulation of a heated granulation mixture containing an active lipophilic substance and a surfactant. The obtained granules are cooled to a semi-solid state and mixed with one or more fillers to cover the surface of the granules. Thereafter, the granules are sieved and tableted.

There are some differences between document C and the present application. Firstly, the application explicitly concerns self-emulsifying or self-dispersing tablets. In order for tablets to self-emulsify or self-disperse when ingested, they should contain a lipid moiety as well as a surfactant. The polyglycerol fatty acid ester in document C provides the surfactant, and according to line 43, page 4, a fatty acid ester may be used in combination with a lipid. Thus, there is reason to believe that granules made according to the scheme of document C would self-emulsify or self-disperse when ingested. Furthermore, the present application concerns tablets, whereas document C only provides granules. This difference, however, is considered to be of minor importance, since the skilled person is familiar with the process of tableting granules, and of the common grain sizes suitable for tableting.

The kernel of the present application is the process of manufacturing of the granules. In this respect, the inventiveness is claimed to be the stepwise sequence of the production, i.e. heating the granulation medium, and cooling the obtained granules to a semi-solid state prior to mixing them with fillers and other excipients. When the granules reach a semi-solid state, it is to be understood that they

.../...

## Supplemental Box

In case the space in any of the preceding boxes is not sufficient.

Continuation of: Box V

have a tacky surface.

The difference between the present application and the process disclosed in document C is the way of obtaining the tacky surface of the granules.

Thus, the problem to be solved by the present application is to find an alternative way of obtaining a tacky surface on granules that contain an active substance and a surfactant.

A person skilled in the art, who realizes that the optimal tackiness of granules occur at a certain temperature, would understand that the granules may reach this temperature during cooling, as well as during heating. Hence, he/she would consider adding fillers and further excipients to the granules during the cooling stage, instead of first cooling the granules and then re-heating them to a predetermined temperature.

Therefore, claims 1-9 lack the requirement of inventive step.

## PATENT COOPERATION TREATY

Rec'd PCT/PTO 19 NOV 2004

10/501873

PCT

From the INTERNATIONAL BUREAU

NOTIFICATION OF THE RECORDING  
OF A CHANGE(PCT Rule 92bis.1 and  
Administrative Instructions, Section 422)

To:

ANKOM

2004 -11- 17

LARFELDT, Helene  
Bergenstråhle & Lindvall  
P.O. Box 17704  
S-118 93 Stockholm  
Sweden

Date of mailing (day/month/year)

05 November 2004 (05.11.2004)

Applicant's or agent's file reference

HeL/AO 49909

## IMPORTANT NOTIFICATION

International application No.

PCT/SE2003/000093

International filing date (day/month/year)

21 January 2003 (21.01.2003)

1. The following indications appeared on record concerning:



the applicant



the inventor



the agent



the common representative

Name and Address

State of Nationality

State of Residence

Telephone No.

Facsimile No.

Teleprinter No.

2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:



the person



the name



the address



the nationality



the residence

Name and Address

State of Nationality

State of Residence

SE

SE

Telephone No.

Facsimile No.

Teleprinter No.

3. Further observations, if necessary:

The person identified in Box 2 should be added to the record as applicant for the United States of America only and inventor for all designated States.

4. A copy of this notification has been sent to:



the receiving Office



the designated Offices concerned



the International Searching Authority



the elected Offices concerned



the International Preliminary Examining Authority



other:

The International Bureau of WIPO  
34, chemin des Colombettes  
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